REMARKS

Claims 3-9, 24-26 and 37 are under consideration in the Office Action. Claims 24, 25 and 37 are amended herein. Claim 3 is cancelled herein. New claims 38-41 are added herein. The amendments add no new matter. After entry of the amendments directed herein, claims 4-9, 24-26 and 37-41 are pending.

Rejection under 35 U.S.C. §102:

Claims 4-9 are rejected under 35 U.S.C. §102(b) as being anticipated by von Arnim et al. as evidenced by Swiss-Prot Database Entry P42212. In the previous Office Action response, Applicants added claim 37, which requires that the first polypeptide is peptide bonded to the second polypeptide "via a linker sequence." All claims were made dependent from new claim 37, such that all claims require the linker sequence. The present Office Action states:

"Applicants urges that, because von Arnim does not teach a linker sequence, the reference does not anticipate the claims.

> This argument has been fully considered but is not deemed persuasive. Although the teachings of von Arnim were not previously applied to claims 2 and 3, which recite the linker limitation, it is clear upon further consideration of the "linker sequence" of the claims that the fusion protein of von Arnim comprises a "linker sequence" as that term is defined in the first paragraph on page 15 of the specification.
>
> The specification states, 'As used herein, the term 'linker sequence' refers to a sequence of peptide bonded amino acids that joins or links by peptide bonds two amino acid sequences or polypeptide domains that are not joined by peptide bonds in nature.' Given the broadest reasonable interpretation of this definition, any amino acid sequence that joins or links two amino acid sequences or domains that are not joined by peptide bonds in nature meets the limitation of a 'linker sequence'. More to the point, the definition does not exclude the middle GFP moiety in the GFP trimer or von Arnim et al. or native GFP amino acid sequence from the meaning of 'linker sequence".

The Office Action thus concludes that the teachings of von Arnim et al. anticipate claims 37 and 4-9. Applicants respectfully disagree.

Applicants have amended claim 37 herein to recite the limitation "via a linker sequence of 5 to 50 amino acids." Support for the amendment is found in claim 3 as filed and in the

specification, e.g., at page 15, lines 5 and 6. Applicants submit that von Arnim et al. does not teach a linker within this size range. Even if one accepts the interpretation that the middle GFP in the GFP trimer taught by von Arnim satisfies the specification's definition of a "linker," the middle GFP monomer is greater than 50 amino acids long.

The Office Action addressed the "5 to 50 amino acids long" limitation in rejecting claim 3, stating that:

> "von Arnim et al. teaches a head to tail fusion resulting in a 'linker sequence' between the 'helix' at amino acids 4 to 8 to the 'strand' at amino acids 217 to 227 (see the NiceProt view of Swiss-Prot: P42212). Thus, the fusion protein of von Arnim et al. comprises a linker sequence of 14 amino acids, which anticipates the limitations of claim 3."

Applicants respectfully disagree with the conclusion that von Arnim et al. teaches a linker of 5 to 50 amino acids.

Applicants submit that where full length polypeptide sequence is fused to full length polypeptide sequence in a "head-to-tail fusion," there is no reason to characterize part of either full length sequence as a "linker" of 5 to 50 amino acids in length. von Arnim et al. states that "Fusion protein genes were constructed based on published *full-length* cDNA sequences using oligonucleotides to introduce suitable restriction enzyme recognition sites" (page 36, left column, last paragraph, emphasis added).

It appears that the Office Action interprets the "helix" and "strand" designations in the Swiss-Prot document as referring to "domains," and then interprets von Arnim's head to tail fusion as joining those two "domains" via the sequence between them, which is apparently interpreted as the "linker" based upon reference to "domains" in the specification's definition of in the specification. Applicants note, however, that claim 37 as amended requires that "said first and said second *polypeptides are monomers of a multimeric fluorescent protein*." In contrast, the Swiss-Prot "domains" identified in the Office Action are a "helix" and a "strand" comprised by a fluorescent monomer. These alleged "domains" are not "monomers of a multimeric fluorescent protein" as required by the claims. The sequence between them cannot, therefore, be a "linker" as the term is used in the claims. Thus, the head-to-tail fusion taught by von Arnim et al. does not teach a "first polypeptide" peptide bonded to a "second polypeptide via a linker sequence of

5 to 50 amino acids" as required by the claims. As such, Applicants submit that von Arnim et al. does not anticipate claim 37 as amended. Reconsideration and withdrawal of the rejection is respectfully requested.

Applicants have added new claims 38-41. New claim 38 recites fusion polypeptides that specifically include a linker selected from the following: (Arg-Ala-Arg-Asp-Pro-Arg-Val-Pro-Val-Ala-Thr)$_{1-5}$, (Gly-Ser)$_{1-15}$, (Thr-Ser-Pro)$_{1-15}$, (Gly-Gly-Gly)$_{1-15}$, (Glu-Lys)$_{1-15}$, and (Gly$_4$Ser)$_{2-4}$. These linker sequences are supported in the specification at, for example, page 26, lines 10-20, and in Figure 4.

New claim 39 relates to fusion polypeptides that have, in addition to the first and second polypeptides that are fluorescent monomers of a multimeric protein, a third polypeptide selected from a transmembrane or intracellular receptor, a cell-surface protein, a growth factor, a signal transduction protein, a transcription factor, a structural protein, an extracellular matrix protein, an immunoglobulin, a bacterial protein, a plant protein, a viral protein, a phage protein, and an enzyme. The language of the claim is supported, for example, at page 27, lines 14-19.

New claims 40 and 41 limit the linkers required in claim 39 respectively to "5 to 50 amino acids in length," which is supported as noted herein above, and one of "(Arg-Ala-Arg-Asp-Pro-Arg-Val-Pro-Val-Ala-Thr)$_{1-5}$, (Gly-Ser)$_{1-15}$, (Thr-Ser-Pro)$_{1-15}$, (Gly-Gly-Gly)$_{1-15}$, (Glu-Lys)$_{1-15}$, and (Gly$_4$Ser)$_{2-4}$", which is also supported as noted herein above.

Allowable subject matter:

The Office Action states that claims 24-26 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants have amended claims 24 and 25 in the suggested manner. Amendment to claim 26 is not necessary, as it depends from amended claim 25.

In view of the above, Applicants submit that all issues raised in the Office Action have been addressed herein. Reconsideration of the claims is respectfully requested.

Respectfully submitted,

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Name: Kathleen M. Williams
Registration No.: 34,380
Customer No.: 27495
Palmer & Dodge LLP
111 Huntington Avenue
Boston, MA 02199-7613
Tel. (617) 239-0100